AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1-32. (Canceled)

33. (Withdrawn–currently amended) ~~The~~ A method of making ~~a~~ the modified GDF-8 propeptide of claim 119 comprising:

(a) preparing a cDNA molecule encoding the modified GDF-8 propeptide of claim 119, wherein the proteolytic cleavage site is ~~modified~~ inactivated;

(b) preparing a cDNA molecule encoding the Fc region of the IgG molecule; and

(c) fusing the cDNA molecules from steps (a) and (b) to produce a modified GDF-8 propeptide.

34. (Withdrawn) The method of claim 33, further comprising preparing a double-stranded oligonucleotide encoding a linker peptide and fusing the cDNA molecules from steps (a) and (b) to either end of the double stranded oligonucleotide encoding the linker peptide.

35. (Withdrawn) The method of claim 33, wherein the linker peptide comprises the amino acid sequence consisting of GSGS.

36-37. (Canceled)

38. (Withdrawn–currently amended) A method of treating a patient suffering from a medical disorder or disease comprising: administering a therapeutically effective amount of a modified GDF-8 propeptide of claim 119 and a pharmaceutically

acceptable excipient to said patient, wherein the modified GDF-8 propeptide has an increased in vivo or in vitro ~~half-life~~ half-life relative to a corresponding unmodified GDF-8 propeptide.

39-41. (Canceled)

42. (Withdrawn) The method of claim 38, wherein the modified GDF-8 propeptide further comprises an Fc region of an IgG molecule.

43. (Withdrawn) The method of claim 42, wherein the IgG molecule is IgG1 or IgG4, or a derivative thereof.

44. (Withdrawn) The method of claim 42, wherein the IgG molecule is IgG1.

45. (Withdrawn) The method of claim 42, wherein the IgG molecule is at least 75% identical to SEQ ID NO:15.

46. (Withdrawn) The method of claim 42, wherein the Fc region of an IgG molecule is identical to SEQ ID NO:15.

47. (Withdrawn) The method of claim 42, wherein the IgG molecule is at least 75% identical to SEQ ID NO:16.

48. (Withdrawn) The method of claim 42, wherein the Fc region of an IgG molecule is identical to SEQ ID NO:16.

49. (Canceled)

50. (Withdrawn) The method of claim 38, wherein the modified GDF-8 propeptide comprises at least one carbohydrate moiety.

51. (Withdrawn) The method of claim 38, wherein the modified GDF-8 propeptide further comprises albumin or a derivative of albumin.

52. (Withdrawn) The method of claim 38, wherein the modified GDF-8 propeptide further comprises a nonproteinaceous polymer.

53. (Withdrawn) The method of claim 38, wherein the medical disorder is a muscular disorder, neuromuscular disorder, metabolic disorder or bone degenerative disorder.

54. (Withdrawn) The method of claim 38, wherein the medical disorder is a muscular or neuromuscular disorder.

55. (Withdrawn) The method of claim 38, wherein the medical disorder is a metabolic disorder.

56. (Withdrawn) The method of claim 38, wherein the medical disorder is amyotrophic lateral sclerosis, muscular dystrophy, muscle atrophy, congestive obstructive pulmonary disease, muscle wasting syndrome, sarcopenia, or cachexia.

57. (Withdrawn) The method of claim 38, wherein the medical disorder is amyotrophic lateral sclerosis or muscular dystrophy.

58. (Withdrawn) The method of claim 38, wherein the medical disorder is obesity, adipose tissue disorder, noninsulin-dependent diabetes mellitus, or type 2 diabetes.

59. (Withdrawn) The method of claim 38, wherein the medical disorder is osteoporosis.

60-118. (Canceled)

119. (Currently amended) ~~An isolated~~ A modified GDF-8 propeptide ~~having at least one~~ comprising:

(a) an amino acid sequence that is at least 75% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a),

wherein the modified GDF-8 propeptide has a mutation in the amino acid sequence ~~at an~~ modifying the aspartate residue corresponding to ~~Asp-99 in SEQ ID NO:1~~ Asp 76 of SEQ ID NO:5, and

wherein the modified GDF-8 propeptide retains one or more biological activities of a GDF-8 propeptide and has an increased in vivo or in vitro half-life relative to a corresponding unmodified GDF-8 propeptide.

120. (Currently amended) The modified GDF-8 propeptide of claim 119, wherein the ~~aspartate~~ residue corresponding to position 76 of SEQ ID NO:5 is ~~mutated to~~ alanine.

121. (Previously presented) The modified GDF-8 propeptide of claim 119 further comprising an Fc region of an IgG molecule.

122. (Previously presented) The modified GDF-8 propeptide of claim 121, wherein the IgG molecule is IgG1 or IgG4.

123. (Previously presented) The modified GDF-8 propeptide of claim 121, wherein the amino acid sequence of the IgG molecule is SEQ ID NO:16.

124. (Previously presented) The modified GDF-8 propeptide of claim 121, wherein the GDF-8 propeptide portion is fused to the Fc region of the IgG molecule via a linker peptide.

125. (Currently amended) The modified GDF-8 propeptide of claim 121, ~~wherein the GDF-8 propeptide has~~ further comprising an altered glycosylation site.

126. (Currently amended) The modified GDF-8 propeptide of claim 121, ~~wherein the GDF-8 propeptide comprises~~ further comprising at least one carbohydrate moiety.

127. (Currently amended) The modified GDF-8 propeptide of claim 119, ~~wherein the GDF-8 propeptide is fused to~~ further comprising albumin.

128. (Currently amended) The modified GDF-8 propeptide of claim 119, ~~wherein the GDF-8 propeptide is fused to~~ further comprising a nonproteinaceous polymer.

129. (Currently amended) The modified GDF-8 propeptide of claim 119, ~~wherein the GDF-8 propeptide is fused to~~ further comprising a second moiety.

130. (Currently amended) The modified GDF-8 propeptide of claim 129, wherein the second moiety is chosen from a protein, polypeptide, carbohydrate, and nonproteinaceous polymer.

131. (Currently amended) The modified GDF-8 propeptide of claim 119, wherein the modified GDF-8 propeptide ~~is fused to~~ further comprises an immunoglobulin molecule, or a fragment thereof.

132. (Previously presented) A pharmaceutical composition comprising the modified GDF-8 propeptide of claim 119 and a pharmaceutically acceptable excipient.

133-136. (Canceled)

137. (Withdrawn–currently amended) A method of treating a mammal comprising administering an effective amount of the pharmaceutical composition of claim 132 ~~or 136~~ to the mammal thereby treating a medical disorder.

138. (Withdrawn) The method of claim 137, wherein the mammal is human.

139. (Withdrawn) The method of claim 137, wherein the medical disorder is a muscular disorder, neuromuscular disorder, metabolic disorder, or bone degenerative disorder.

140. (Withdrawn) The method of claim 137, wherein the medical disorder is chosen from amyotrophic lateral sclerosis, muscular dystrophy, muscle atrophy, congestive obstructive pulmonary disease, muscle wasting syndrome, sarcopenia, cachexia, type 2 diabetes, noninsulin-dependent diabetes mellitus, hyperglycemia, obesity, and osteoporosis.

141. (Withdrawn) A method of inhibiting GDF-8 activity comprising contacting GDF-8 with the modified GDF-8 propeptide as in any one of claims 119-131.

142. (Withdrawn–currently amended) A method of increasing muscle mass in a mammal comprising administering an effective amount of the modified GDF-8 propeptide as <u>in</u> any one of claims 119-131 to the mammal, thereby increasing muscle mass.

143. (Canceled)

144. (New) An modified GDF-8 propeptide comprising

(a) a GDF-8 moiety comprising

(i) an amino acid sequence that is at least 75% identical to SEQ ID NO:5 or

(ii) a biologically active fragment of the amino acid sequence of (a), and

(b) an optional heterologous moiety,

wherein the GDF-8 moiety has a mutation in the amino acid sequence at the residue corresponding to position 76 of SEQ ID NO:5, and

wherein the modified GDF-8 propeptide retains one or more biological activities of a GDF-8 propeptide and has an increased in vivo or in vitro half-life relative to a corresponding unmodified GDF-8 propeptide.

145. (New) The modified GDF-8 propeptide of claim 144, wherein the mutation in the amino acid sequence at the residue corresponding to position 76 of SEQ ID NO:5 in the GDF-8 moiety is a substitution mutation.

146. (New) The modified GDF-8 propeptide of claim 145, wherein the residue corresponding to position 76 of SEQ ID NO:5 is alanine.

147. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence that is at least 75% identical to SEQ ID NO:5.

148. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence that is at least 80% identical to SEQ ID NO:5.

149. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence that is at least 85% identical to SEQ ID NO:5.

150. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence that is at least 90% identical to SEQ ID NO:5.

151. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence that is at least 95% identical to SEQ ID NO:5.

152. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety comprises an amino acid sequence identical to SEQ ID NO:5, except that it has a mutation at the residue corresponding to position 76 of SEQ ID NO: 5.

153. (New) The modified GDF-8 propeptide of claim 144, wherein the GDF-8 moiety consists of

(a) an amino acid sequence that is at least 75% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a).

154. (New) The modified GDF-8 propeptide of claim 153, wherein the GDF-8 moiety consists of

(a) an amino acid sequence that is at least 80% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a).

155. (New) The modified GDF-8 propeptide of claim 153, wherein the GDF-8 moiety consists of

(a) an amino acid sequence that is at least 85% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a).

156. (New) The modified GDF-8 propeptide of claim 153, wherein the GDF-8 moiety consists of

(a) an amino acid sequence that is at least 90% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a).

157. (New) The modified GDF-8 propeptide of claim 153, wherein the GDF-8 moiety consists of

(a) an amino acid sequence that is at least 95% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a).

158. (New) The modified GDF-8 propeptide of claim 153, wherein the GDF-8 moiety consists of

(a) an amino acid sequence identical to SEQ ID NO:5, except that it has a mutation at the residue corresponding to position 76 of SEQ ID NO: 5, or

(b) a biologically active fragment of the amino acid sequence of (a).

159. (New) The modified GDF-8 propeptide of claim 158, wherein the residue corresponding to position 76 of SEQ ID NO:5 is alanine.

160. (New) The modified GDF-8 propeptide of claim 144, wherein the heterologous moiety is chosen from a protein, polypeptide, carbohydrate and nonproteinaceous polymer.

161. (New) The modified GDF-8 propeptide of claim 144, wherein the heterologous moiety comprises an immunoglobulin molecule, or a fragment thereof.

162. (New) The modified GDF-8 propeptide of claim 161, wherein the heterologous moiety comprises an Fc region of an IgG molecule.

163. (Previously presented) The modified GDF-8 propeptide of claim 162, wherein the IgG molecule is IgG1 or IgG4.

164. (Previously presented) The modified GDF-8 propeptide of claim 162, wherein the amino acid sequence of the IgG molecule is SEQ ID NO:16.

165. (New) A modified GDF-8 propeptide comprising

(a) an amino acid sequence that is at least 75% identical to SEQ ID NO:5, or

(b) a biologically active fragment of the amino acid sequence of (a), and

wherein the modified GDF-8 propeptide has an amino acid other than aspartate at the residue corresponding to position 76 of SEQ ID NO:5, and

wherein the modified GDF-8 propeptide retains one or more biological activities of a GDF-8 propeptide and has an increased in vivo or in vitro half-life relative to a corresponding unmodified GDF-8 propeptide.

166. (New) The modified GDF-8 propeptide of claim 165, wherein the residue corresponding to position 76 of SEQ ID NO:5 is alanine.

167. (New) The modified GDF-8 propeptide of claim 165, wherein the modified GDF-8 propeptide further comprises an immunoglobulin molecule, or a fragment thereof.

168. (New) The modified GDF-8 propeptide of claim 165, wherein the modified GDF-8 propeptide further comprises an Fc region of an IgG molecule.

169. (Previously presented) The modified GDF-8 propeptide of claim 168, wherein the IgG molecule is IgG1 or IgG4.

170. (Previously presented) The modified GDF-8 propeptide of claim 168, wherein the amino acid sequence of the IgG molecule is SEQ ID NO:16.

171. (New) A modified GDF-8 propeptide comprising a non-human GDF-8 propeptide homolog of SEQ ID NO:5 chosen from bovine, dog, cat, chicken, murine, rat, porcine, ovine, turkey, baboon, and fish,

wherein the modified GDF-8 propeptide has an amino acid other than aspartate at the residue corresponding to position 76 of SEQ ID NO:5, and

wherein the modified GDF-8 propeptide retains one or more biological activities of a GDF-8 propeptide and has an increased in vivo or in vitro half-life relative to a corresponding unmodified GDF-8 propeptide.